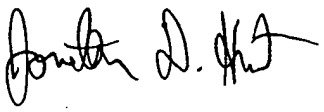
with 37 C.F.R. 1.822(d)(4), the numbering of SEQ ID NOs:37-39 have been amended to begin at residue "1" rather than "216." Amendments to the specification have been made to keep conformity between amended sequence listing and the numbering of residues referred to in the specification. Thus, it will be understood that these amendments constitute no new matter.

Additionally, the amino acids referred to in claims 5 to 7 are not restricted to the sequence listing, but are generic positions as would be understood by one of ordinary skill in the art in light of the teachings of the specification. One of ordinary skill in the art would recognize that the Kabat sequence listing provides a standard format for the numbering of conserved regions within molecules of immunological interest. One of ordinary skill would further recognize that listing specific residues in accordance with Kabat provides the requisite teaching for analogous modifications of any immunoglobulin. The modification of the specific residues taught by the specification leads directly to an increase in the serum half-life of an immunoglobulin molecule. This modification should not be considered applicable only to the sequences set forth in the SEQ ID NOs:37-39, but rather that this molecule provides a template upon which such modifications may be modeled for other Ig species. One of skill would recognize that the Kabat reference simply supplies a system of nomenclature that enables the application of the modifications made in one template to increase the serum half-life of other immunoglobulin molecules. Therefore, SEQ ID NOs:37-39 has been provided solely to illustrate what positions in the Ig molecule the numbering refers to rather than to limit the scope of the invention to a single murine IgG species.

Included with this response is an amended sequence listing, an additional hard copy, a computer readable form, and a declaration by the undersigned attorney for the Applicant, asserting that the amendment includes no new matter.

The Examiner is invited to contact the undersigned patent agent at 512-418-5674 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



Jonathan D. Hurt
Reg. No. 44,790
Agent for Applicant

ARNOLD, WHITE & DURKEE
P.O. Box 4433
Houston, Texas 77210-4433
(512) 418-3000

Date: January 13, 2000

APPENDIX A

1. A composition comprising a mutant IgG molecule having an increased serum half-life relative to IgG, and wherein said mutant IgG molecule has at least one amino acid substitution in the Fc-hinge region.

2. The composition of claim 1, wherein said IgG is a human IgG.

3. A composition comprising a mutant IgG Fc-hinge fragment having an increased serum half-life relative to the serum half-life of IgG, and wherein said fragment has an increased binding affinity for FcRn.

4. A composition comprising a mutant IgG Fc-hinge fragment having an increased serum half-life relative to the serum half-life of IgG, and wherein said fragment has the same or slightly lower affinity than IgG for binding to FcRn.

5. The composition of claim 1 or 3, wherein said molecule or fragment has an amino acid substitution at one or more of the amino acids selected from number 252, 254, 256, 309, 311, or 315 in the CH2 domain or 433 or 434 in the CH3 domain.

6. The composition of claim 5, wherein said molecule or fragment has three amino acid substitutions at amino acid number 252, 254, 256, 309, 311, or 315 in the CH2 domain or 433 or 434 in the CH3 domain.

7. The composition of claim 6, wherein said molecule or fragment has the following amino acid substitutions: leucine for threonine at position 252, serine for threonine at position 254 and phenylalanine for threonine at position 256.

8. The composition of claim 1 or claim 3, wherein said molecule or fragment has a dissociation constant for binding to FcRn at pH 6, of less than about 7 nM as measured by surface plasmon resonance analysis.

9. The composition of claim 1 or claim 3 further defined as a pharmaceutically acceptable composition.

10. The composition of claim 5, wherein said amino acid substitutions are generated by random mutagenesis.